REMARKS

Status of the Claims

Claims 64, 65, 68-103 and 132-144 are pending.

Claims 71, 73, 76-90, 136-139 and 144 have been withdrawn from consideration.

Claims 64, 65, 68-70, 72, 74, 75, 91-103, 132-135 and 140-143 have been rejected.

By way of this amendment, claims 64, 65, 68, 72, 74, 75, 91-103, and 132-135, which are under consideration, have been amended, claims 76-90, 136-139, and 144 have been canceled, and new claims 145-165 have been added. In addition, withdrawn claims 71 and 73, have been amended.

Upon entry of this amendment, claims 64, 65, 68-75, 91-103, 132-135, 140-143 and 145-165 will be pending.

Summary of the Amendment

Claims 64, 65, 68, 72, 74, 75, 91-103, and 132-135, and withdrawn claims 71 and 73 have each been amended to change term "ST receptor" to "guanylyl cyclase C". Guanylyl cyclase C is the more precise and accepted scientific name for the receptors referred to in the claims. The specification at page 1, lines 17-19, and page 14, lines 23-25 clearly indicates that the terms are intended to be used interchangeably.

Claims 64 and 65 have also been amended to delete the phrases "substantially continuous" and "per hour for a period of time" and to correct an grammatical error by changing the "induces" to the term "induce."

Claim 68 has been amended to clarify that the therapeutic agent expressly referred to therein is a "different" therapeutic agent from the guanylyl cyclase C ligand. It is clear from Example 1 of the specification that applicants' invention included monotherapies using guanylyl cyclase C ligand as well as combination therapies using guanylyl cyclase C ligand in combination with other therapeutic agents.

Claims 74 and 134 have been amended to clarify that the antibody fragments are "guanylyl cyclase C binding fragments." The specification at page 15 lines 3 and 4 clearly indicate that the term "ST receptor ligand" is intended to refer to compounds which specifically bind to the ST receptor. Page 22 lines 20 and 21 of the specification clearly reflect that ST receptor ligands include anti-ST receptor antibodies. Page 26, lines 14-17 and 21-22, clearly reflect that the term antibody is intended to include antibody fragments. Thus, the specification discloses that ST receptor ligands are compounds that specifically bind to the ST receptor. ST receptor ligands can be antibodies; such antibodies, to be ST receptor ligands, must bind to ST receptors. Since antibodies is clearly intended to refer to intact antibodies as well as antibody fragments, the intact antibodies and antibody fragments must bind to ST receptor to be ST receptor ligands.

New claims 145 and 146 are dependent on claims 75 and 135, respectively, and further define the guanylyl cyclase C ligand as being a humanized anti-guanylyl cyclase C antibody. New claims 145 and 146 read on the elected species. Support for new claims 145 and 146 is found on page 26, lines 23 and 24.

New claims 147-165 correspond to claims 68, 69, 71, 72, 74, 75, 91-102 and 145, respectively, except that they are dependent on claim 103.

Applicants have amended the specification on page 63, line 10, to correct an obvious typographical error.

Applicants have amended the paragraph beginning on page 12, line 20, to correct obvious typographical errors.

No new matter has been added.

Restriction Requirement

In Applicants' Response to March 5, 2007 Restriction Requirement , Applicants believe an error was made in indicating that claim 70 read on the elected species. Specifically, Applicants indicated that claim 70 referred to the elected mode of administration. Applicants note that claim 71, not claim 70, reads on the elected mode of administration. Claim 70 reads on a non-elected different species of therapeutic agent. Applicants respectfully request that claim 71, which reads on the elected species be rejoined for examination at this time.

Drawings

The Drawings are objected to as failing to comply with 37 C.F.R. § 1.84(p)(5) because they fail to incorporate reference signs "2d – 2f." Applicants have prepared and attached herewith Replacement Drawings of Figures 1 through 4 pursuant to 37 C.F.R. § 1.121(d). The Replacement drawings correctly identify panels 2d, 2e, and 2f. Applicants have also replaced the reference signs on Figures 1, 3, and 4 with reference signs that are more clear. No new matter has been added to the drawings.

Applicants respectfully request that the objection to the Drawings be withdrawn.

Specification

The Specification has been objected to for a typographical error on page 63. Applicants have amended the specification on page 63, line 10, to correct an obvious typographical error.

Applicants respectfully request that the objection to the Specification be withdrawn.

Rejections under 35 U.S.C. 112, second paragraph

Claim 64, 65, 68-70, 72, 74, 75, 91-103, 132-135 and 140-143 have been rejected under 35 U.S.C. 112, second paragraph as failing to particularly point out and distinctly claim the subject matter of the claimed invention.

Claims 64 and 65 have been amended to delete the terms "substantially continuous" and "per hour for a period of time".

Claim 68 has been amended to clearly recite that the therapeutic agent expressly referred to in the claim is a different therapeutic agent that the guanylyl cyclase C ligand referred to in claims 64 and 65.

Claims 74, 75, 134 and 135 have been amended to recite that the antibody fragments referred to in the claims bind to guanylyl cyclase C.

Claim 133 has been amended to clearly recite that the guanylyl cyclase C binding moiety is conjugated to an active moiety.

As amended, the claims are clear and definite. Applicants respectfully request that the rejection be withdrawn.

Rejections under 35 U.S.C. 112, first paragraph

Claim 64, 65, 68-70, 72, 74, 75, 91-103, 132-135 and 140-143 have been rejected under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement..

It is asserted that the claimed subject matter is not enabled because one skilled in the art would not predict that the claimed invention would be operable in vivo in view of the in vitro data presented in the specification. Moreover, it is asserted that one skilled in the art would not predict that the claimed invention related to the use of antibodies as therapeutic agents would be effective. Applicants respectfully disagree.

The in vitro experiments set forth in the specification accurately describe the mechanism by which guanylyl cyclase C effect cells, thereby allowing one skilled in the art to use such compounds to achieve the claimed effect in vivo. One skilled in the art would expect that the invention would be effective in vivo in view of the in vitro data. The cited art relied upon in the Official Action present a general case of questioning the extrapolation of in vitro data to in vivo

effectiveness. However, these references do not address specific instances where the mechanism for action is demonstrated at the level of detail and understanding set forth in the instant specification.

As for the predictability of antibody therapeutics, Applicants assert that at the time the invention was made, one skilled in the art would have accepted that the claimed subject matter would be effective. The references cited in the Official Action refer to the unpredictability of drugs with initial anti-cancer activity emerging as a clinically effective therapy. Applicants urge that there are many reasons for failures of anti-cancer drugs to become commercially useful products. The standards by which a drug is evaluated for commercial use is different from simply whether or not it is operable in the context of patent law. The mere failure of drugs to not proceed to commercialization does not indicate it does not work to the level needed to establish patentability. Thus, it is improper to rely on the statistics of failed drug development as supporting a rejection that the subject matter would not be enabled under the requirements of the patent law.

Conclusion

Claims 64, 65, 68-75, 91-103, 132-135, 140-143 and 145-165 are in condition for allowance. A notice of allowance is earnestly solicited.

The Commissioner is hereby authorized to charge any deficiencies of fees and credit of any overpayments to Deposit Account No. 50-0436.

Respectfully submitted,

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Attachment: Replacement Sheets (Figures 1-4)